REMARKS

Claims 38, 40, 41, 43, 45, 46, 49 and 65-68 are pending and stand rejected under 35 U.S.C. §§ 101, 112, first paragraph (written description and enablement) and 112, second paragraph.

Claim 38 has been amended as shown above to replace "control element" with "promoter." This amendment was inadvertently omitted from Applicants previous response. Inasmuch as the amendment corrects improper antecedent basis, it does not raise new issues for consideration and, indeed, simplifies the issues for appeal. Accordingly, entry of this amendment after final is requested.

35 U.S.C. §101

Claims 38, 40, 41, 43, 45, 46, 49, and 65-68 were again rejected under 35 U.S.C. §101 as allegedly lacking utility. (Final Office Action, pages 2-6).

Again while acknowledging there is a well-establishing utility set forth in the specification, the Examiner nonetheless asserts (Office Action, page 6, emphasis in original):

> The problem is that the asserted utility of using the mouse or method to study gene expression applies only to those experimental systems that recapitulate **native** gene expression, and the claims are not directed to/**limited to** such constructs/experimental systems.

As a threshold matter, Applicants submit the claims are in fact limited to functional promoters, namely by the fact that the promoter is operably linked to the sequences encoding a light-generating protein.

In any event, a utility rejection should not be imposed where there is a well-established utility and/or where there is one credible utility (*see,* M.P.E.P. § 2107, emphasis added):

> If at any time during the examination, **it becomes readily apparent that the claimed invention has a well-established utility, do not impose a rejection based on lack of utility**. ...
>
> (1) If the applicant has asserted that the claimed invention is useful **for any particular practical purpose** (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art, **do not impose a rejection based on lack of utility**.

> ... An applicant need only provide **one** credible assertion of specific and substantial utility for each claimed invention to satisfy the utility requirement.

In other words, a utility rejection cannot be based on an allegation that the claims are somehow "overly broad."

Therefore, in the pending case, Applicants are not required to limit their claims to promoters that recapitulate native gene expression in order to show utility, because a well established utility has been acknowledged for these embodiments and because the claims are limited to promoters that are operably linked to sequences encoding light-generating proteins. As such, withdrawal of this rejection is in order.

35 U.S.C. §112, First Paragraph, Written Description

Claims 38, 40, 41, 43, 45, 46, 49 and 65-68 were again rejected on the grounds that Applicants' specification fails to sufficiently describe the claimed transgenic mice. (Final Office Action, pages 6-7). In particular, it was alleged that the "specification has not described those constructs that will provide for native gene expression." (Final Office Action, page 7)

It remains the case that satisfaction of the written description requirement does not require either working examples showing particular constructs or a listing in the specification of particular exemplary constructs. This is because the constructs are assembled from known sequences.

The Federal Circuit has completely rejected the notion that the specification must describe information (*e.g.,* nucleotide sequence) for a chimeric molecule in which the individual components are known (*See, e.g., Capon v. Eshhar* 76 USPQ2d 1078, 1085 (Fed. Cir. 2005), emphasis added):

> The "written description" requirement must be applied in the context of the particular invention and the state of the knowledge. **The Board's rule that the nucleotide sequences of the chimeric genes must be fully presented, although the nucleotide sequences of the component DNA are known, is an inappropriate generalization.** When the prior art includes the nucleotide information, precedent does not set a *per se* rule that the information must be determined afresh. Both parties state that a person experienced in the field of this invention would know that these known DNA segments would retain their DNA

> sequences when linked by known methods. Both parties explain that their invention is not discovering which DNA segments are related to the immune response, for that is in the prior art, but in the novel combination of the DNA segments to achieve a novel result.
>
> The "written description" requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution.

As in *Capon,* the nucleotide sequences of (1) stress-inducible promoters and (2) sequences encoding light-generating proteins were well-known at the time of filing (and described in the specification). Moreover, as in *Capon,* the skilled artisan would know that these known sequences would retain their sequences when linked by known (and described) methods.

Thus, as in *Capon,* the invention lies not in discovering the particular constructs including stress-inducible promoters, but in the novel combination of these promoters and light-generating protein-encoding sequences to achieve a novel result, namely transgenic animals as claimed. Accordingly, the written description requirement is satisfied with respect to the claimed subject matter.

35 U.S.C. §112, First Paragraph, Enablement

The Examiner again maintains that undue experimentation would be required in order to practice the invention of claims 38, 40, 41, 43, 45, 46, 49 and 65-68. (Final Office Action, pages 7-8). As noted in their previous responses, ample evidence of enablement has been submitted, including Declarations and publications establishing that making a transgenic mouse including two or more constructs as claimed is fully enabled by the as-filed specification.

As set forth in the seminal case of *In re Marzocchi,* 439 F.2d, 220, 223, 169 USPQ 367, 369 (CCPA 1971), a patent application is presumptively enabled when filed:

> [a]s a matter of Patent Office practice ... a specification .. must be taken as in compliance with the enablement requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

Moreover,

> it is incumbent upon the Patent Office, whenever a rejection on [grounds of enablement] is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure.

439 F.2d at 224, 169 USPQ at 369-370. Indeed, as pointed in the Patent Office's own Training Manual on Enablement (1993, citing *In re Wright,* 999 F.2d 1557, 1561-1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993), "the case law makes clear that properly reasoned and supported statements explaining any failure to comply with section 112 are a requirement to support a rejection."

The Examiner has not properly set forth why the teachings of the specification do not enable one of skill in the art to make and use the claimed mice. The Office has not provided any reason to doubt that the same methods that are used to make transgenic mice comprising a single construct can be used to make a mouse comprising two or more constructs, especially given the evidence of record establishing that multiple construct-containing transgenic mice have been generated using these methods.

It is not sufficient for the Examiner to assert, without supporting evidence, that the cited articles are not relevant. In the absence of evidence supporting the allegation that making such mice was "highly unpredictable" at the time of filing, the rejection cannot be maintained.

Applicants have repeated their arguments for the simple reason that they establish satisfaction of the enablement requirement. Methods of making transgenic mice comprising a single construct were routine at the time of filing; the specification teaches one of skill in the art how to make and use animals including two or more constructs; and the art teaches that multiple construct-containing mice are made in the same way as single construct-containing mice. Accordingly, one of skill in the art would conclude that following the teachings of the specification for single construct animals would also work, without modification, for transgenic mice as claimed.

Thus, Appellants have provided ample factual evidence demonstrating that the specification enables the pending claims throughout their scope and the rejection should be withdrawn.

35 U.S.C. § 112, 2nd Paragraph

Claims 38, 40, 41, 45, 46, 49 and 65-68 were rejected under 35 U.S.C. § 112, 2nd paragraph as indefinite because claim 38 recited "said second control element." (Office Action, page 8).

As noted above, Applicants inadvertently did not amend claim 38 in their previous response so that all recitations of "control element" were changed to "promoter". Applicants have corrected this unintentional omission by amendment above, thereby obviating the rejections under 35 U.S.C. § 112, 2nd paragraph. Accordingly, the rejection can be properly withdrawn.

CONCLUSION

Applicant respectfully submits that the claims comply with the requirements of 35 U.S.C. §112 and define an invention that is patentable over the art. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

If the Examiner notes any further matters that the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned at (650) 493-3400.

Respectfully submitted,

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